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THE CHEMICAL BASIS OF LIFE

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IT was in 1868 that Professor Huxley, in Edinburgh, that city of intellectual light, made the memorable declaration for the first time in a formal fashion that life has a physical basis; this substance was at that time known as "protoplasm," it has since been named "bioplasm"; but it was the notion that life should have a physical basis at all that was unfamiliar to the biological laity at the end of the sixties. This notable declaration, especially from its having been made on a Sunday evening, was the subject of not a little acrimonious comment.

Life without a physical basis is unknown to science, whatever may be conceivable by the human mind. But the concept to which I now wish to advance is, that the time has come for us to realize that it would be more accurate to speak of the *chemical*, rather than "the physical basis of life." From the most general point of view that we can take, it must be obvious that no kind of matter, non-living, dead, or alive, can possibly exist outside the realm of the operation of the laws of chemical affinity. From this exceedingly wide conception there certainly flow several very important consequences related to our thesis, but my present standpoint is rather this, that what we know as the various manifestations of vitality are conditioned by, or actually related to, the precise chemical configuration or constitution of this substance—the so-called protoplasm.

Now this is not a truism: it is not self-evident that the same laws which govern purely chemical operations in the laboratory should govern in precisely the same way phenomena which we have always called vital. It is more intensely true that life is a chemical rather than a physical affair; for does not life depend in an exceedingly intimate fashion on the chemical affinity between oxygen and hæmoglobin as well as on the chemical affinity for oxygen possessed by the living matter which can only subsist by constantly incorporating that gas within it? Life is, in a very real sense, oxidation; but what is oxidation other than the chemical union of oxygen and certain other chemical elements—carbon, hydrogen, sulphur, or phosphorus—wherever these elements happen to be found? Oxygen is in a very real sense the *gaseous* basis of life.

It is equally true that digestion, for instance, is a chemical affair; it can proceed to a certain point as efficaciously in a glass vessel as inside the living stomach, and it is influenced in the glass vessel by agents and agencies in exactly the same way as it is in the living body: alcohol, for instance, slows the process in both cases.

But there is a school of physiologists which would go farther and assert that nutrition (assimilation) is from first to last a purely chemical affair, that it depends on the affinities of certain molecules of food for certain molecules of protoplasm. That great vital cycle which may be said to begin with the discharge of animal waste-products, which are then fermented by bacteria into the nitrate food for plants, are worked up by these plants into their food-reserves, are eaten by herbivora, which are eaten by ourselves, is, in each link of it, chemical; either a synthesis or a decomposition. The reason that gelatine by itself will not support life has been discovered to be that it does not contain a substance of some chemical complexity, tyrosin, found in all other nitrogenous food. That one man's food is his neighbour's poison must depend upon the chemical constitution of their tissues.

Or again, evidence is accumulating every day that the explanation of fatigue is a problem in organic chemistry; a fatigued person is one in whose body-fluids are circulating in solution certain "katabolites," as they are called, bodies derived from the living matter as the result of its prolonged activity. These are at present merely known as "fatigue-toxins," and fatigue is therefore called toxæmia, which is only the Greek for blood-poisoning, but that these toxins have a definite, though possibly complex, chemical constitution is beyond the possibility of a doubt.

What is happening other than a chemical union between the cat and the chloroform when we end its earthly existence? It is purely a matter of organic chemistry; we have saturated the molecules of the living cat by means of those of the non-living chloroform to such a degree that that manifestation of vitality, the cat's consciousness, has vanished. In other words, life can be chemically extinguished; and this is what is done every time there is poisoning by alcohol or the cyanides or perchlorides *et hoc genus omne*.

"Dutch courage" is a chemical affair; its basis, purely chemical and capable of being quantitatively estimated, is alluded to in the lines of Burns—

"Wi' tippeny we fear nae evil,
Wi' usequebagh we'd face the deevil."

When a person has become bad tempered through an attack of gout, or sleepy through an attack of jaundice, or sick from an attack of dyspepsia, or from having taken apomorphine, only a chemical explanation can be a complete one.

Now nothing is more familiar to the student of elementary chemistry than that heat facilitates and cold retards the activity of a chemical process, but it is equally well known to the student of elementary physiology that heat facilitates and cold retards the activity of a vital process. This does not indeed amount to a formal proof of the identity of life and chemical action, but it constitutes a high probability that they have something essential in common. When we make the remark that red-haired persons are usually irritable, we assert something that cannot mean that red hair in itself is the cause of bad temper. There must underlie both red hair and bad temper some one common antecedent chemical condition. That hair should be red instead of black or brown is a question of the chemistry of melanin; and the chemical peculiarity in the skin which is expressed as redness of hair must be intimately related to some other chemical peculiarity of the nervous system which expresses itself as irritability in the mental condition of the person in question. The absence of pigment from the skin and hairs of certain animals (albinos) is known to be associated with certain chemical peculiarities of their blood.

Or take the case of our sensations, always regarded as indubitable evidences of life. The vividness of these, even their very existence, can be made to depend on purely chemical conditions; the application of cocaine will abolish the sensation of pain, the chewing of gymnema sylvestre will abolish the taste of bitter things, while the taking of chloroform or of alcohol can modify or abolish certain sensations altogether. The toxins of fatigue have a distinct influence on the intensities of sensation, the tired person fails to perceive a certain phenomenon quite obvious to one whose nervous system is fresh.

The central proposition, however, is that bioplasm behaves essentially in the same fashion as a chemical substance does, that its activity is influenced by agents and agencies in the same manner as is a compound of high chemical instability. In support of this there is the noteworthy fact that living matter is constantly producing heat as the result of oxidations. This heat cannot have other than a chemical origin; it is indeed "vital" heat, but it is as truly chemical. It can be none other than the heat produced by the oxidation of carbon to carbon dioxide, of hydrogen to water, of sulphur to sulphuric acid, of phosphorus to phosphoric acid, all of which chemical substances we know to be constantly leaving the body. This animal heat is not physical; that is, it is not due to friction or to condensation of gas, but is as chemical as the heat set free when dilute sulphuric acid is poured upon zinc. Animal heat, so far from being, as the ancients thought, heat of an order entirely its own, is indistinguishable from heat of chemical origin. But if protoplasmic heat is of chemical origin, then *the* characteristic of life (evolution of heat) is a phenomenon within the realm of the laws of chemical activity. Indeed, Professor Rubner of Berlin, has shown that the animal body yields to a calorimeter in a given time almost exactly the same quantity of heat as would have been produced by the actual combustion of the food digested within that period.

Our next reason for believing that living matter behaves essentially as a chemical substance, is the way in which, as has been hinted, it is affected by a rise or fall of temperature. A fall of temperature depresses the energy of chemical unions, immobilizes molecules, makes all transformations of elements or of ions less easily accomplished; in a word, tends to create a condition of chemical inertness. Many chemical reactions and double decompositions which are suppressed altogether by a low temperature, are at ordinary temperatures quite feasible. Now protoplasm reacts towards cold in a precisely similar fashion. Cold depresses its activity, reduces the intensity of its energy-manifestations, immobilizes its molecules and generally inhibits its activity. This most familiar fact can only mean that vitality is lessened or suppressed because the molecular whirl of the living stuff has been profoundly interfered with or abolished. The muscles of our hands and face become "stiff with cold" because the chemical activities of the muscles are depressed by the cold, the molecules literally immobilised. The converse of all this is to be observed as regards heat. A rise of temperature accelerates the velocity of chemical reactions and in many cases carefully studied, does so to the extent of doubling the velocity for each rise of ten degrees centigrade. Now all biologists know that precisely the same thing is true of protoplasm; its activities are not only accelerated by a rise of temperature, but, in a number of cases studied as to time-relations, the same law of doubled effect for a rise of ten degrees has been observed to be obeyed. All this looks exceedingly like heat acting on a chemical substance.

In confirmation of this mode of viewing living matter we have the special case of what has been well called latent life. In this state the chilled or dried bioplasm is *not* dead, for it can revive to activity on the temperature rising or on water being supplied to it, but neither is it alive, since it is exhibiting none of the evidences of vitality—evolution of heat, carbon dioxide, and water. It is merely capable of yielding once more these evidences of vitality, and it can exhibit a brief electric current on the reception of a brief electric stimulus (Waller's "last sign of life"). It is potentially but not actually alive. But this complete arrest of vital manifestations without death of the protoplasm can only be explained in terms that are chemical. It is the exact analogue of those chemical substances which have been cooled or dried to such a degree that they have become quite inert in a chemical sense. Chemists recognize chemical inertia, physiologists have been forced to recognize physiological inertia. It admits of no doubt whatever that a substance continually capable of eliminating water, carbon dioxide, sulphuric acid, phosphoric acid, and urea must be a chemical substance. Now protoplasm does actually eliminate these compounds. Tissue-respiration and the production of animal heat cannot have other than a chemical basis. Living matter behaves in a typically chemical fashion as regards its affinities for certain elements capable of coming into union with it. In the healthy state it has been shown, for instance, that it is impossible to oversaturate the tissue with oxygen, iron, arsenic, iodine, sodium, or any other element. There is a certain power of combining with these substances possessed by the tissues, and beyond that affinity-limit the bioplasm cannot be coerced into taking up any more oxygen, or iron, or arsenic, or iodine, or sodium, or any other element. This peculiarity is explicable only on the assumption that the substance protoplasm has a structure determined by the conditions which determine the properties of all substances which react *inter se;* namely, the combining-powers of the different species of matter endowed with chemical affinities. This fixedness of limit for saturation of protoplasm by chemical substances explains the impossibility of indefinite increase in bulk of the nitrogenous tissues by over-feeding with nitrogenous food, of increasing the intensity of tissue-changes to any notable extent by the breathing of pure oxygen or of increasing, for instance, the iron- or phosphorus-content of the healthy red-marrow or brain. This possession of affinities for particular substances must be the explanation of the incorporation of drugs and poisons, and indeed of all food material itself: if this did not exist, no drug could be absorbed and no poison fixed in the tissues, which is only the chemical manner of saying that no drug could affect and no poison injure the body. Since poisons and food are absorbed, chemical affinity between the living matter and the food or drug is an absolute necessity. Researches are now being made, particularly by Dr. A. D. Waller, on the quantity of poisonous substance which can be fixed in a muscle in order to produce a definite result, for instance the abolition of its contraction. In this way, then, chemical substances are responsible for modifying or abolishing vitality.

But again, we have been forced to recognize a particular type of sleep as that of auto-intoxication by soluble substances alluded to provisionally as "fatigue-toxins": this type is often and quite properly described as sleep of *chemical* origin. It is the chemical effect on the brain-cells related to consciousness of substances produced by previous tissue-activity. In order to influence the brain-cells these toxins must for a time be chemically incorporated with the cerebral molecules, conceivably as "side-chains" (Ehrlich), and subsequently be subjected to oxidative elimination during sleep. It has for some time been recognized that bodily fatigue is chemical; the fatigue factor in sleep is necessarily no less so.

The objective aspect of fatigue in the nervous system has been minutely studied of late years, with the result that certain phosphorus-containing granules in the nerve-cells have been identified as the material basis of the energy production. When these granules are of a certain contour, recognized as "normal," the cells are fresh or "fit" in common parlance, able to discharge their nerve-energy (neurine); in exhausted states the granules are visibly altered, shrunken, etc. It is their chemically complex constitution that enables them to be the seats of dynamogenesis, apparently nothing chemically simpler than this kinetoplasm would suffice.

That tissues habitually act chemically is recognized in the expression quite familiar to all physiologists since the time of Claude Bernard—"chemical tone." This is only a more definite expression than "tissue tone," and it denotes that state of well-being of the tissues when each one is doing its duty in the best, that is in the most economical, way possible. The secreting gland-cells are in chemical tone when, supplied with the necessary amount of blood but no more, they manufacture aright their ferments and other secretions and send them with the proper amount of force towards the ducts, while they give to the lymph certain waste substances not needed by the cells and indeed deleterious to them if retained. Possibly the term "chemical tone" has arisen because in muscle there is a physical tone as well as a chemical, or rather the tone of muscle is capable of a double expression—(1) a certain tension of the fibres (incipient contraction) and evolution of heat which may be called the factors in physical tone, and (2) a certain state of chemical fitness or chemical tone shown by the evolution of carbon dioxide. Flabbiness is due to a loss of physical tone, chilliness and diminished excretion of carbon dioxide are due to the loss of chemical tone. The supposition that both sorts of tone are maintained by innervation, though an extremely interesting topic, does not enter into our present subject.

It is due to the discoveries in biochemistry of the last few years that we regard tissue-tone as dependent on the well-being of, it may be, quite distant organs. Thus, there is no doubt that muscle-tone is maintained by a chemical substance manufactured by the apparently insignificant suprarenal capsules. If they are diseased or extirpated the heart becomes notably weaker and the body muscles reduced in tonicity: this action is said to be carried out by an "internal secretion." Similarly, it has been demonstrated that the thyroid gland has a distinct influence on the skin and nervous system, the most debilitating condition known as myxœdema being produced when this comparatively small gland is diseased. Other still smaller glands have equally important controlling powers, the pituitary, as it is called, at the base of the brain, controls bone-formation in such a way that if it is diseased in early life the person grows up to be a giant. The profound influence exerted on the whole organism by the development of the sex glands is so familiar a fact in physiology that it need not be more than mentioned here.

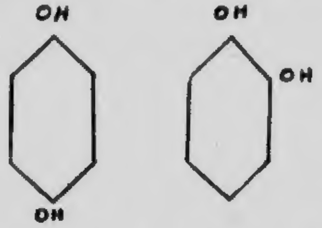
The differences in chemical constitution of the different tissues must be the reason why, for instance, in the child the growing bone absorbs more lime than does any other tissue, the nervous system more phosphorus; the blood-corpuscles more potassium and iron, the cartilages more sodium, and so on: each tissue must possess selective affinities in order that the precise chemical structure should not become a merely haphazard occurrence. Further, the potassium of blood-corpuscles cannot be replaced by sodium or lime indifferently; not only the same elements must remain in the tissues in order that they be in health, but precisely the same percentage of them, each for each. Professor Loeb, of Chicago, and many before him and after him, have shown that most minute changes in the concentration of the inorganic salts, the ions, bathing the various living tissues affect the health of these tissues in what would appear a quite disproportionate fashion. Certain marine eggs will not develop properly if immersed in a solution of salts differing only exceedingly slightly from normal sea water. Monsters a/ and aberrant forms in the case of the simpler aquatic creatures can be artificially produced by thus tampering with the chemical constitution of the saline nutrient media for the eggs.

Certain diseased conditions seem related in some little understood fashion to the chemical constitution of tissues. Scurvy is due to a deficient absorption of potassium, rickets to that of calcium, a form of anæmia to that of iron, all chemical aberrations: gout and all that flows from it, is very largely an affair of the insufficient excretion or the over-production of sodium and calcium urate. Why there should be deficient absorption and deficient excretion, respectively, must be susceptible of only a chemical explanation. In gastric cancer there is deficient excretion of hydrochloric acid. It is very familiar that certain diseases have favourite seats of attack, the toxin of diphtheria, for instance, selects the muscles of the palate, of tetanus certain cell-groups in the nervous system, of hydrophobia certain other cell-groups in the nervous system, the poison of syphilis has a distinct predilection for the bones, the skin, and the central nervous system; the reason for these selective affinities must be ultimately a chemical one.

Similarly the most curious tendencies for certain drugs and poisons, both mineral and vegetable, to be absorbed by certain tissues—digitalis by heart-muscle, arsenic by bone-marrow and skin, strychnin by cells of the central nervous system, atropin by nerve-endings, nicotin by motor nerve-endings, chloroform by the cells related to consciousness,—must have an explanation that is wholly chemical: every day we are getting nearer to what it is.

The aberrant metabolism of calcium in old age with increase of it in the rib cartilages, in the larynx, and in the walls of arteries, as also the silting up of the membrana tympani with calcic salts is a chemical affair.

To pass to totally different examples: the realm of the sensations affords us several examples of the dependence of life on chemical conditions. Allusion has already been made to the modification of sensations by means of the presence of fatigue, drugs, and diseased conditions, but there is a department of the physiology of the senses devoted to the study of a relationship between the sensations and the chemical configuration of sensation-arousing substances. Thus, many years ago, Professor Haycraft of Cardiff, pointed out that if one arranged certain substances in order of their atomic weights, it was possible to show that their smell-producing and taste-producing powers were a function of their atomic weights. He demonstrated that the presence or absence of an atom of carbon or of hydrogen made considerable difference to the odour or taste of the bodies under examination. Since the date of this paper, a good deal of observation has been made on similar lines, and it is now known that, for instance, the mere position, whether symmetrical or not, of the hydroxyl groups in the benzene ring, determines the sweetness or bitterness of a compound, thus:—



the former being the bitter quinol, the latter the sweet catechol.

There is not much difference chemically between these two bodies, and what there is is entirely stereochemical, but the sweet and bitter-perceiving end-organs are evidently perfectly pre-adapted to be affected differently by the extremely slight alteration in the relative place of the side-chain.

We have evidence that such lowly living creatures as the fungi are exceedingly susceptible to such infinitesimal differences as those between a substance and its isomer. Certain sugars, able to be fermented by certain yeasts, are quite unable to be attacked by other but closely allied yeasts. Or again, a given yeast will readily ferment a sugar while totally unable to deal with another sugar of precisely the same percentage composition, but differing from the former only in having its hydroxyl groups relatively differently arranged in the chain.

Chemical constitution, nay, the possession of the element phosphorus, is an important factor in a subject so difficult of comprehension as heredity. Biologists seem to be in no doubt that the substance concerned in the transmission from parent to offspring of the potentialities of certain physical and psychical attributes is what the morphologists call chromatin, the chemists nucleo-protein. A high percentage of phosphorus is a characteristic of nucleoprotein, so that it is literally true that our existence chemically depends on the phosphorus of this absolutely microscopic substance. The fusion of the female nucleus with the male nucleus or sperm must depend on certain mutual chemical affinities operative whenever these two complementally endowed portions of living matter are enabled to come within a certain distance of each other.

But if this much be admitted, then it must follow that the congenital differences and the inherited peculiarities which distinguish the one sex from the other and one social stratum from the other, are, in ultimate analysis, based on chemical differences. There are no discernible differences between the physical organs and tissues of the coal-heaver and the sovereign; but it is inconceivable that there is not some real, specific, though undiscoverable, difference in the ultimate *chemical* constitution of the living matter of the two men, enough chemical difference to account for that comparatively small difference in their social behaviour which is denoted by the word "breeding."

While undoubtedly Huxley was right in teaching at the time he did that life had a physical basis, it seems to me interesting, if not as important, to realize that it also and as truly has a chemical one. While I have thus emphasized, it may be thought unduly, the resemblances between living matter and non-living substances capable of exhibiting chemical activity, and while I believe that the same laws govern the behaviour of carbon, and hydrogen, and oxygen, whether they are in living muscle or in dead muscle, or in sugar or in gunpowder, yet I should regret it exceedingly if I were understood to support the crude generalization that the realms of life and of chemical phenomena are indistinguishable and coextensive. Far be it from me to suggest that the crucibles and condensers of our chemical laboratories contain the secret of the mystery of vitality or of consciousness.